PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 205332251	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. **PCT/AU2004/000509**	International filing date *(day/month/year)* 16 April 2004	Priority date *(day/month/year)* 17 April 2003

International Patent Classification (IPC) or national classification and IPC

Int. Cl. [7] C08B 37/08, 37/06, 37/04, 37/02, 31/10, 9/00, 11/04, 37/00, A61K 31/738, A61P 43/00

Applicant

ULTRACEUTICALS R&D PTY LIMITED et al

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 3 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. [X] *(sent to the applicant and to the International Bureau)* a total of **3** sheets, as follows:
      - [X] sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      - [ ] sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. [ ] *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or table related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - [X] Box No. I Basis of the report
   - [ ] Box No. II Priority
   - [ ] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - [ ] Box No. IV Lack of unity of invention
   - [X] Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - [ ] Box No. VI Certain documents cited
   - [ ] Box No. VII Certain defects in the international application
   - [ ] Box No. VIII Certain observations on the international application

Date of submission of the demand 16 November 2004	Date of completion of the report 8 June 2005
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **G. D. HEARDER** Telephone No. (02) 6283 2553

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/AU2004/000509

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1 (b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

☐ the international application as originally filed/furnished

☒ the description:

pages **1-16** as originally filed/furnished
pages* received by this Authority on with the letter of
pages* received by this Authority on with the letter of

☒ the claims:

pages **17** as originally filed/furnished
pages* as amended (together with any statement) under Article 19
pages* **18-20** received by this Authority on **5 May 2005** with the letter of **5 May 2005**
pages* received by this Authority on with the letter of

☒ the drawings:

pages **1/3-3/3** as originally filed/furnished
pages* received by this Authority on with the letter of
pages* received by this Authority on with the letter of

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages
☐ the claims, Nos.
☐ the drawings, sheets/figs
☐ the sequence listing (*specify*):
☐ any table(s) related to the sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages
☐ the claims, Nos.
☐ the drawings, sheets/figs
☐ the sequence listing (*specify*):
☐ any table(s) related to the sequence listing (*specify*):

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-34	YES
	Claims		NO
Inventive step (IS)	Claims	1-34	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-34	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The following documents identified in the International Search Report have been considered for the purposes of this report:

D1	WO 2000/046253	D5	FR 2 717 815
D2	WO 1987/007898	D6	WO 2002/038614
D3	CA 1,315,464	D7	GB 2 151 244
D4	CA 2 416 504	D8	JP 05-140201

Claims 1-34

No individual citation or obvious combination of citations disclose the features of the claims

12. The process according to any one of claims 1 to 11 wherein the optional washing step (c) further comprises washing the cross-linked polysaccharide matrix with acetone.

13. The process according to any one of claims 1 to 12 wherein the neutralisation step (d) further comprises freeze drying the cross-linked polysaccharide gel and reconstituting the gel.

14. The process according to claim 13 wherein the freeze dried cross-linked polysaccharide gel is reconstituted in phosphate buffered saline.

15. The process according to any one of claims 1 to 14 further comprising combining the polysaccharide with a biologically active substance.

16. A cross-linked polysaccharide gel substantially resistant to hyaluronidase degradation prepared by the process according to any one of claims 1 to 15.

17. The gel according to claim 16 wherein the gel releases less than about 75 percent uronic acid under hyaluronidase treatment.

18. The gel according to claim 16 wherein the gel releases no more than about 70 percent uronic acid under hyaluronidase treatment.

19. The gel according to claim 16 wherein the gel releases no more than about 65 percent uronic acid under hyaluronidase treatment.

20. The gel of claim 16 wherein the gel releases less than about 75 percent uronic acid after being extruded or expelled from a 32 gauge needle.

21. The gel according to claim 16 wherein the gel releases no more that about 70 percent uronic acid after being extruded or expelled from a 30 gauge needle.

22. The gel according to any one of claims 16 to 21 further comprising a biologically active substance.

23. The gel according to claim 22 wherein the biologically active substance is a hormone, cytokine, vaccine, cell, tissue augmenting substance, or mixture thereof.

24. The gel according to claim 23 wherein the tissue augmenting substance is collagen, starch, dextranomer, polylactide, poly-beta-hydroxybutyrate, or copolymers thereof.

25. The gel according to claim 22 wherein the biologically active substance is an alkaloid, peptide, phenothiazine, benzodiazepine, thioxanthene, hormone, vitamin, anticonvulsant, antipsychotic, antiemetic, anesthetic, hypnotic, anorexigenic, tranquilizer, muscle relaxant, coronary vasodilator, antineoplastic, antibiotic, antibacterial, antiviral, antimalarial, carbonic anhydrase inhibitor, nonsteroid antiinflammatory agent,

vasoconstrictor, cholinergic agonist, cholinergic antagonist, adrenergic agonist, adrenergic antagonist narcotic antagonist or combination thereof.

26. A pharmaceutical composition comprising:

a cross-linked polysaccharide gel according to claim 16;

a biologically active substance; and

a pharmaceutically acceptable carrier.

27. A pharmaceutical composition comprising:

a biocompatible gel according to any one of claims 16 to 21;

a biologically active substance; and

a pharmaceutically acceptable carrier.

28. The pharmaceutical composition according to claim 26 or 27 wherein the preparation is in the form of a pill, tablet, capsule, suppository, spray, cream ointment or sticking plaster.

29. A method of treating or preventing a disorder or condition selected from the group consisting of tissue augmentation, arthritis, tissue adhesions, immunogenicity, diseases of the mucosa, dermatological conditions, ophthalmological conditions, hormonal conditions, joint lubrication conditions and cosmetic conditions, in a subject in need thereof, comprising administering a therapeutically effective amount of a gel according to any one or more of claims 16 to 25.

30. A method of treating or preventing a disorder or condition selected from the group consisting of tissue augmentation, arthritis, tissue adhesions, immunogenicity, diseases of the mucosa, dermatological conditions, ophthalmological conditions, hormonal conditions, joint lubrication conditions and cosmetic conditions, in a subject in need thereof, comprising administering a therapeutically effective amount of a pharmaceutical composition according to any one of claims 26 to 28.

31. The method according to claim 29 or 30, wherein the administration to the subject is by injection.

32. The method according to claim 29 or 30, wherein the administration to the subject is by topical application.

33. Use of a gel according to any one or more of claims 16 to 25 for the manufacture of a medicament for treating or preventing a disorder or condition selected from the group consisting of tissue augmentation, arthritis, tissue adhesions, immunogenicity,

diseases of the mucosa, dermatological conditions, ophthalmological conditions, hormonal conditions, joint lubrication conditions and cosmetic conditions, in a subject in need thereof.

34. Use of a pharmaceutical composition according to any one of claims 26 to 28 for the manufacture of a medicament for treating or preventing a disorder or condition selected from the group consisting of tissue augmentation, arthritis, tissue adhesions, immunogenicity, diseases of the mucosa, dermatological conditions, ophthalmological conditions, hormonal conditions, joint lubrication conditions and cosmetic conditions, in a subject in need thereof.